DOI:
10.1007/s11469-013-9447-0

Document Version
Peer reviewed version

International Journal of Mental Health & Addiction

A national survey investigating methadone treatment for pregnant opioid dependent women

--Manuscript Draft--

Manuscript Number:	
Full Title:	A national survey investigating methadone treatment for pregnant opioid dependent women
Article Type:	Regular Article
Keywords:	Methadone; Community Drug Treatment Services; Pregnant; opioid dependent.
Corresponding Author:	Raul Perez-Montejano, M.D, Ph.D Tees, Esk and Wear Valleys NHS Foundation Trust Northallerton, UNITED KINGDOM
Corresponding Author Secondary Information:	
Corresponding Author's Institution:	Tees, Esk and Wear Valleys NHS Foundation Trust
Corresponding Author's Secondary Institution:	
First Author:	Raul Perez-Montejano, M.D, Ph.D
First Author Secondary Information:	
Order of Authors:	Raul Perez-Montejano, M.D, Ph.D
	Emily Finch, M.D
	Kim Wolff, PhD
Order of Authors Secondary Information:	

Abstract

We investigated the management and treatment of pregnant opioid users by Drug Treatment Services by region across England and Wales. A postal survey was conducted among 223 Community Drug Treatment Services (CDTS) across England and Wales. Sixty-six percent CDTS responded (n=154/233) to the survey. Over half CDTS (55.3%) provided a maintenance methadone dose lower than that recommended for non-pregnant drug users. There were significant variations across regions and how professionals approached the management of pregnant opioid users. CDTS with an addiction specialist were significantly more likely ($p<.01$) to advocate high doses of methadone whereas those with a midwife, obstetrician or social worker involved were more likely ($p<.05$) to suggest low dose methadone and/or detoxification. Service provision for pregnant opioid users is reliable and comprehensive but there is still variability in some aspects of the treatment received and the way in which methadone is prescribed is not always optimal.

Keywords: Methadone, Community Drug Treatment Services, Pregnant, opioid dependent.

Introduction

In the UK there has been a steady increase of births to pregnant drug users from an estimated 568 births reported in 1995 (Morrison & Siney, 1995), rising to 1, 057 births in 2003 (Advisory Council on the Misuse of Drugs, 2003) and 1, 970 in 2007 (Lakhani, 2009). Methadone for the treatment of opioid dependence in pregnancy has remained controversial since its early introduction in the 1960s with researches debating the benefits for the treatment of this complex group. However, methadone maintenance treatment has been the consensus adopted by the United States (Centre for Substance Abuse Treatment, 2009), Australia (New South Wales Department of Health, 2006), and the UK (Department of Health (England) and the devolved administrations, 2007) for the management of pregnant opioid dependent women. Nevertheless the benefits of methadone for the treatment of this group has remained controversial (McGlone, Mactier, & MacKinnon, 2008). Research pertaining to the effectiveness of methadone during pregnancy has been wide ranging but rarely systematic (Jones, O'Grady, Malfi, & Tuten, 2008). Ethical considerations coupled with cost have severely restricted the number of investigations that adequately covers the pre-, peri- and post-natal periods (Wolff, Boys, Rostami-Hodjegan, Hay, & Raistrick, 2005). There have also been conflicting findings on fetal, neonatal and maternal outcomes of methadone maintained pregnant opioid users (DePetrillo & Rice, 1995; Drozdick, Berghella, Hill, & Kaltenbach, 2002; Hagopian et al., 1996; Kempley, 1995; Winklbaur et al., 2008). Arguments, supporting either high dose methadone during pregnancy (to avoid opioid withdrawal and fetal distress or relapse to illicit drug use), or challenging the benefits of this strategy by advocating low dose pharmacotherapy or detoxification (to reduce the occurrence of neonatal withdrawal), continue to be made (Nunn et al., 2009; Maas, Kattner, Weingart-Jesse, Schafer, & Obladen, 1990).

The UK Goverment Home Office, Professional and Non-Professional bodies, the Royal College of General Practitioners (Ford et al., 2005) and the Local Government Drugs Forum (ILGDF/SCODA), (Local Goverment Drugs Forum/Standing Conference on Drug Abuse. LGDF/SCODA, 1997) have suggested the need for integrated care. The 2007 UK Department for Health 'Drug Misuse and Dependence: UK Guidelines on Clinical Management 2007' (Department of Health (England) and the devolved administrations, 2007) however contained little direct information for the management and treatment of pregnant drug users. And although the more recent National Institute for Health and Clinical Excellence (NICE) guidelines on pregnancy (National Institute for Health and Clinical Excellence (NICE), 2010) addressed many of the issues surrounding the provision of services for this complex group, its remit did not include pharmacotherapy for opioid dependence during pregnancy.

There is international consensus on the effectiveness of fixed daily doses of between 60-120mg methadone for dependent drug users (Faggiano, Vigna-Taglianti, Versino, & Lemma, 2003), however, there is no such accord for those who are pregnant. This creates an unnecessary ambiguity for the clinician who faces a dosing dilemma; the benefits of high dose methadone against its possible association with a neonatal abstinence syndrome (NAS). Little has been recorded in England and Wales about prescribing practices for opioid dependent addicts who become pregnant. In light of the absence of information about this vulnerable population we investigated the provision of services for pregnant opioid dependent women and in particular how Community Drug Treatment Services (CDTS) address the issue of pharmacotherapy.

Method

A list of 387 different drug treatment services across England and Wales was identified from Drugscope's helpfinder (www.drugscope.org.uk/resources/helpfinder -

accessed October 2006). Those that did not provide prescribing services including services for young people, rehabilitation centres, special population services and prison services were excluded. As a result, 233 Community Drug Treatment Services (CDTS) were identified as the target population. A coded bespoke questionnaire was distributed via postal address to the managers of the CDTS in three different mailings between November 2006 and May 2007. The questionnaire sought information about service structure (capacity and professionals involved), current policies within the organisation, management and pharmacotherapy for pregnant opioid users. Ethical approval was obtained from the Joint South London & Maudsley NHS Foundation Trust and Institute of Psychiatry Research Ethics committee (Ref 299/03 COREC 04/Q0705/22).

Statistical analysis

Descriptive and chi square modelling was used for the first stage of the analysis and chi square testing and one by one correlational techniques used for comparing binary variables. Difference between CDTS was also assessed for statistical significance using Mann-Whitney U-test or Kruskal-Wallis as appropriate. Logistic regression models were used to determine factors that influenced service provision (service demographics, staff profession, number of clients and prescribing policy etc). In contingency tablets larger than 2X2, a chi-square test was used if fewer than 20% of the expected frequencies were less than five and no expected frequency was less than one. Where this requirement was not met the recommendation of Siegel and Castellan (Siegel & Castellan, 1988) and others (Bland, 1987; Kirkwood, 1988) was followed and, wherever appropriate, categories were combined to reduce the number of cells to a 2x2 table thus increasing the expected frequencies. This recommendation was used particularly to compare regions when contingency tables were 10 x 2 and the chi-square test revealed a significant difference but assumptions were not met.

Results

Sixty-six percent of CDTS managers (n = 154/233) responded to the survey representing 8 key regions in England & Wales (see Table 1). Seventy three percent of CDTS reported treating ≤ 10 pregnant drug users at any one time (40% treating ≤ 5). At the time of the survey the remaining 27% CDTS reported having >10 pregnant opioid addicts in their service.

Service provision

A considerable proportion of pregnant drug users were already known to CDTS and/or presented during the first trimester of pregnancy (72.5%). Only a small minority (7.4%) reported referrals as a consequence of a late presentation of pregnancy. Most women (81.2%) self-referred although managers also reported referrals from GPs (73.4%), antenatal clinics (68.8%), social services (57.8%) and the criminal justice/probation service.

Service Structure

The composition of CDTS varied but predominantly comprised a prescribing doctor (96%), and drug and alcohol nurses (89.5%); many CDTS reported having a pregnancy addiction specialist (60%), who was often a drug and alcohol nurse (77.2%). Sixty-four CDTS (42%) reported having a specialist clinic for pregnant drug users In addition, almost half CDTS had a drug counsellor (48.4%) and/or a drug worker (43%). Clinical Psychologists (CP) and Community Psychiatric Nurses (CPN) were also reported as part of the team (32.0% and 31.4%, respectively). Service managers reported having close links with community midwives (83.0%), obstetricians (65.4%) and social services (65.4%).

Methadone

Methadone pharmacotherapy was the treatment of choice (97.4%, 148/152) for pregnant women whilst buprenorphine (67.8%) was also commonly prescribed but only 35% of CDTS offered ‘maintenance’ dosing to pregnant women, and 10.6% stabilization followed

by detoxification (see Figure 1). Induction onto methadone varied: 53.6% managers reported initial dosing of between 30-40 mg methadone/day and others (21.9%) <30mg methadone/day Most CDTS (70.2%) advocated methadone maintenance treatment (MMT) for opioid dependent pregnant women. Two strategies for MMT were apparent; maintenance of a fixed daily dose ≤ 50 mg methadone/day (55.3%, CDTS) or prescription of the lowest possible fixed daily dose (52.8%, CDTS). CDTS with pregnancy addiction specialists and/or drug counsellors were twice (OR 2.61 v OR 2.19) as likely to recommend MMT regardless of the presenting dose ([X^2 (1, n=150) = 7.09, P <.008, Phi=.217] and [X^2 (1, n=151) = 4.64, P <031, Phi=.175], respectively). Compared to other CDTS those who reported a higher proportion of midwife involvement were 2.38 times more likely [X^2 (1,n=150)= 3.98, P <046, Phi=.163] to advocate low daily dosing with methadone.

One third of managers (33.6%) reported that their service had a 'high- dose' policy for pregnant women: reporting a total mean maximal dose of 138mg (SD $\pm$ 35.7mg) methadone/day. CDTS that shared care with non-specialist midwives reported prescribing a significantly (P <014) lower maximum daily dose of methadone (median 120 mg/day). Most CDTS (93.2%) reported that they would increase the daily dose of methadone if a pregnant woman complained of opioid withdrawal symptoms during the third trimester, with 91.4% prescribing increments of between 5-10 mg methadone/day. Managers reported that CDTS also recommended splitting the daily methadone dose (61.9%); and some advocated alternative therapies (13.6%, 20/147). A small number advised 'coping' with opioid withdrawal symptoms rather than offer an intervention (6.1%, 9/147).

Many CDTS (65.5%) also employed gradual methadone dosage reduction during pregnancy. A policy of methadone stabilisation followed by detoxification was reported by 34.4% of CDTS managers. The odds of receiving this dosage regime was significantly greater (OR 3.16 v OR 3.19) if midwives [X^2 (1, n=150)= 4.33, P<037, Phi=.170,] or if

neonatologists [X^2 (1, n=150)= 9.72, P <002, Phi=.255,] were involved in treatment planning. Prescribing decisions were also influenced by concern about the neonatal abstinence syndrome (NAS). Of those services (41%) that believed the onset and severity of NAS were associated with methadone dose, the majority (96.5%) had a policy of prescribing <30 mg day. Services that had an in-house policy for pregnant women were significantly more likely [X2 (1, N=134) = 3.91, P < 048, Phi = -174] to report that there was no association between methadone dose and NAS and prescribed higher doses

Community-based opioid detoxification was offered by 23.8% of CDTS overall and inpatient opioid detoxification by 37% CDTS. Inpatient detoxification was significantly associated with the involvement in the service of neonatologists [X^2 (1, n=150) = 6.43, P <.011, Phi=.207, OR= 2.55], specialist liaison midwives [X^2 (1, n=150)= 5.34, P <021, Phi=.188, OR= 2.22] or social workers [X^2 (1, n=150)= 4.48, P <034, Phi=.172, OR= 2.18]. The model containing both neonatologists and social workers was significant [.X^2 (2,N=150) = 9.72, P <008) and explained between 6.3% (Cos and Snell square) and 8.6% (Nagelkerke R squared) of the variance in flexibility with methadone dosing and correctly classified 67.3% of managers responses. However, only the variable *'neonatologist'* made a unique statistically significant contribution to treatment and when a neonatologist was involved CDTS were 2.28 times more likely to offer inpatient detoxification.

Buprenorphine

Although buprenorphine was commonly prescribed (67.8%) for pregnant opioid dependent women, only 35% of CDTS offered 'maintenance' dosing, and even fewer (10.6%) stabilization followed by detoxification.

Benzodiazepines

Many CDTS (60%) reported prescribing benzodiazepines to pregnant drug users. There was a significant association (*P* <027) between having an in-house clinic specifically

for pregnant women and prescribing benzodiazepines. CDTS with a pregnancy addiction specialist were twice (OR= 2.18) as likely to prescribe benzodiazepines as those without an appointed in-house specialist service [X^2 (1, n=149) = 6.84 P <027, Cramer's V= .18].

Discussion

This is the first study to investigate the treatment provision, by CDTS, offered to pregnant opioid users in England and Wales. Service managers reported that CDTS were multidisciplinary in nature and heterogeneous in composition. Integrated care services such as those reported here are advocated as an effective model of care in the UK (National Institute for Health and Clinical Excellence (NICE), 2010; Becker & Duffy, 2002), and indeed practice in many areas was very good with the majority of pregnant opioid users accessing CDTS and antenatal services during their first trimester. Overall CDTS appeared to have the necessary competences to provide a service for this complex population. MMT was the treatment of choice for the majority of CDTS in line with the UK National guidelines, which at the time recommended "low dose maintenance for pregnant opioid users" (pp 82, 1999) (Department of Health (England) and the devolved administrations, 1999) later amended to *"maintenance at a dose that stops or minimises illicit use" (pp 81 7.4.7.1; 2007)* (Department of Health (England) and the devolved administrations, 2007). However, dosing decisions by some CDTS were significantly different from the national guidelines and at odds with the scientific evidence, with implications for maternal and fetal outcome. Dosing strategy was largely dependent upon the professional profile of the treatment service. For instance, the role of both the neonatologist and the social worker was significant [.X^2 (2, N=150) = 9.72, P <008) and classified 67.3% of managers responses.

Although treatment practices have been investigated internationally [18, 28-29], little has been reported about community-based services for pregnant women in the United Kingdom. The Advisory Council on the Misuse of Drugs (ACMD) (Advisory Council on the

Misuse of Drugs, 2003) described the provision of services for this complex group in 2003 however, only 20% of respondents to that survey were prescribing services. This CDTS survey was conducted on a nationally representative sample where sampling error was minimised by selecting only community-based services that provided substitute pharmacotherapy. In addition, a response rate of 66% was achieved overall which is above the response rate considered acceptable for self-completion questionnaires (Sitzia & Wood, 1998). Selection bias may have been present amongst those service managers who chose to take part but this was thought unlikely since this study substantiates work conducted on individual clinics in the field. The survey was however conducted just prior to the publication of the 2007 National guidelines (Department of Health (England) and the devolved administrations, 2007), although these were not significantly different from those published in 1999 (Department of Health (England) and the devolved administrations, 1999).

Even though methadone detoxification during pregnancy has remained controversial, this approach was frequently reported by CDTS managers. Both inpatient (offered by 37% CDTS) and outpatient (24% CDTS) detoxification and detoxification following stabilisation (34% CDTS) were reported. Opioid detoxification has been contra-indicated in both the first trimester of pregnancy because of the risk of miscarriage and in the last trimester because of the possibility of precipitating pre-term labour, fetal distress, and even stillbirth (Department of Health (England) and the devolved administrations, 2007). However, Young (Young, 2007) revealed that the underlying evidence was tentative at best and based on two case studies that had low scientific power (n = 1) and no controls (Rementeria & Nunag, 1973; Zuspan, Gumpel, Mejia-Zelaya, Madden, & Davis, 1975). The Royal College of General Practitioners', using evidence from a comparison of two self-selected Scottish groups (Hepburn, 1997), suggest that methadone detoxification can be carried out *'at any speed and at any stage'* during pregnancy (Ford et al., 2005). Others highlight nevertheless the poor

maternal treatment outcomes observed following opioid detoxification, such as the high rate of relapse back to illicit drug use (Kashiwagi, Arlettaz, Lauper, Zimmermann, & Hebisch, 2005), which has been widely observed to be detrimental to neonatal outcomes (Hulse, Milne, English, & Holman, 1997; Unger et al., 2011). In this survey the likelihood of a CDTS recommending inpatient detoxification was doubled (0R = 2.28) when neonatologists, were involved in patient care. The rationale for this treatment approach was not reported but it may have been that neonatologists like other clinicians, sought to err on the side of caution and advocate detoxification to avert the fear of fetal sedation or NAS. Variability in the way that national drug policy is interpreted was evident from our respondents, a finding that substantiates qualitative research in the UK (Klee, 2002), which reports that conflicting advice is given to pregnant opioid users by different healthcare professionals. Further work is required to establish the effectiveness of methadone detoxification for this population.

High-dose MMT during pregnancy, on the other hand, has been associated with positive outcomes such as ‘normal’ gestational birth weight and head circumference (Hagopian et al., 1996; Hulse et al., 1997; Wittmann & Segal, 1991), reduced neonatal complications and a shorter period of hospitalisation (Igboekwu & Wolff, 2010). Indeed leading researchers in North America advocate a policy of high-dose therapy for pregnant opioid users (Drozdick et al., 2002). In the UK, the 2007 NICE guidelines: ‘Methadone and buprenorphine for the management of opioid dependence’ (National Institute for Health and Clinical Excellence (NICE), 2007), recommended fixed daily dosing of 60 to 110 mg methadone as optimal therapy for opioid dependent addicts. Evidence from North America suggests that these dosage regimes could be safely applied to pregnant women in the UK, who demonstrate appropriate severity of dependence, yet only a third of our CDTS had a high-dose MMT policy. Decisions concerning high doses were significantly more likely when healthcare professionals with specialist knowledge such as pregnancy addiction

specialists and addiction counsellors (OR 2.61 and OR 2.19, *P* <008, respectively) were involved, suggesting that expertise and training is important for the care of these women. There was greater consistency of care concerning withdrawal symptom complaints during the last trimester of pregnancy with 93% CDTS advising pharmacological intervention and/or division of the daily dose However, practice elsewhere has not followed this policy and in Scotland, with multiple agency support, women reportedly managed dosage reductions in the later stages of pregnancy, without clinical intervention (Hepburn, 2002).

More systematic work is required to familiarise healthcare professionals, policy makers and commissioners with the evidence that demonstrates the benefit of high-dose of MMT during pregnancy. Keeping drug addicts in treatment is accepted by the UK National Audit Office as being cost-effective; saving £1 for every £2.50 spent on treatment (National Audit Office, 2010; Barnard, Webster, O'Connor, Jones, & Donmall, 2009). Furthermore, in the interests of maternal and infant welfare definitive evidence must be gathered that abstinence is sustainable in the post natal period following detoxification treatment. Although prescribing decisions are, by their nature individually formed, advocates of detoxification may overestimate the ability of the newly abstinent mother to cope with child rearing as well and the process of recovery from a chronic relapsing condition. Research in the British context of the community-based drug treatment service should be urgently commissioned to clarify dosing strategies for pregnant addicts, replicating North American work if necessary. Further consideration also needs to be given to the influence of different disciplines in prescribing decisions and more stringent efforts should be made to ensure that all healthcare professionals involved in the care of pregnant opioid dependent women are aware and work within the national clinical guidelines for substance misuse and dependence. There remain many conflicting messages remain for those charged with the care of pregnant opioid users and a need for consensus on how to manage this population is urgently required.

Reference List

Advisory Council on the Misuse of Drugs (2003). *Hidden Harm: Responding to the Needs of Children of Problem Drug Users* London: Home Office.

Barnard, M., Webster, W., O'Connor, W., Jones, A., & Donmall, M. (2009). *The Drug Treatment Outcome Research Study (DTORS), Key Findings* (Rep. No. 26). Home Office.

Becker, J. & Duffy, C. (2002). *Women Drug Users and Drug Service Provision: service-level responses to engagement and retention.* Home Office Drugs Strategy Directorate.

Bland, M. (1987). *An introduction to Medical Statistics*. Oxford: Oxford University Press.

Centre for Substance Abuse Treatment. (2009). Substance Abuse Treatment: Addressing the Specific Needs of Women. Treatment Improvement Protocol (TIP) Series 51. HHS Publication No. (SMA) 09-4426.Rockville,MD: Substance Abuse and Mental Health Services Administration.

Department of Health (England) and the devolved administrations (1999). *Drug Misuse and Dependence: UK Guidelines on Clinical Management.* London: Department of Health (England), the Scottish Government, Welsh Assembly Government and Northern Ireland Executive.

Department of Health (England) and the devolved administrations (2007). *Drug Misuse and Dependence: UK Guidelines on Clinical Management*. London: Department of Health (England), the Scottish Government, Welsh Assembly Government and Northern Ireland Executive.

DePetrillo, P. B. & Rice, J. M. (1995). Methadone dosing and pregnancy: impact on program compliance. *International Journal of the Addictions, 30,* 207-217.

Drozdick, J., Berghella, V., Hill, M., & Kaltenbach, K. (2002). Methadone trough levels in pregnancy. *American Journal of Obstetrics and Gynecology, 187,* 1184-1188.

Faggiano, F., Vigna-Taglianti, F., Versino, E., & Lemma, P. (2003). Methadone maintenance at different dosages for opioid dependence (Review). *Cochrane Database of Systematic Reviews 2003*.

Ford, C., Barnard, J., Bury, J., Carnwath, T., Gerada, C., Joyce, A. et al. (2005). Special Groups. Pregnancy. In *Guidance for the use of methadone for the treatment of opioid dependence in primary care* (First ed., pp. 16-17). London: Royal College of General Practitioners.

Hagopian, G. S., Wolfe, H. M., Sokol, R. J., Ager, J. W., Wardell, J. N., & Cepeda, E. E. (1996). Neonatal outcome following methadone exposure in utero. *J.Matern.Fetal Med., 5,* 348-354.

Hepburn, M. (1997). Drugs of addiction. In F.Cockburn (Ed.), *Advances in Perinatal Medicine* (pp. 120-124). Carnforth: Parthenon Publishing.

Hepburn, M. (2002). Drug Use and Women's Reproductive Health. In T.Petersen & A. Mc Bride (Eds.), *Working with Substance Misusers, A Guide to Theory and Practice* (pp. 285-295). London: Routledge.

Hulse, G. K., Milne, E., English, D. R., & Holman, C. D. (1997). The relationship between maternal use of heroin and methadone and infant birth weight. *Addiction, 92,* 1571-1579.

Igboekwu, J. & Wolff, K. (2010). Methadone maintenance therapy and feto-maternal outcomes of pregnancy. *Heroin Addiction and Related Clinical Problems, 12,* 17-22.

Jones, H. E., O'Grady, K. E., Malfi, D., & Tuten, M. (2008). Methadone maintenance vs. methadone taper during pregnancy: maternal and neonatal outcomes. *Am.J Addict., 17,* 372-386.

Kashiwagi, M., Arlettaz, R., Lauper, U., Zimmermann, R., & Hebisch, G. (2005). Methadone maintenance program in a Swiss perinatal center: (I): Management and outcome of 89 pregnancies. *Acta Obstet.Gynecol.Scand., 84,* 140-144.

Kempley, S. (1995). Methadone maintenance treatment. Pregnant women taking methadone should be warned about withdrawal symptoms in babies. *BMJ, 310,* 464.

Kirkwood, B. (1988). *Essentials of medical statistics*. Blackwell Scientific Publications.

Klee, H. (2002). Drugs and Pregnancy. In H.Klee, M. Jackson, & S. Lewis (Eds.), *Drug misuse and motherhood* (pp. 78-92). Oxon: Routledge.

Lakhani, N. (2009). More babies are born drug dependent. *Addiction Today,* 2-3.

Local Goverment Drugs Forum/Standing Conference on Drug Abuse. LGDF/SCODA (1997). *Drug Using Parents: Policy Guidelines for inter-agency working.* LGDF.

Maas, U., Kattner, E., Weingart-Jesse, B., Schafer, A., & Obladen, M. (1990). Infrequent neonatal opiate withdrawal following maternal methadone detoxification during pregnancy. *J Perinat.Med., 18,* 111-118.

McGlone, L., Mactier, H., & MacKinnon, J. R. (2008). Outcome in infants exposed to methadone in utero. *BMJ, 337,* a1774.

Morrison, C. & Siney, C. (1995). Maternity services for drug misusers in England and Wales: a national survey. *Health Trends, 27,* 15-17.

National Audit Office (2010). *Tackling problem drug use, Report by the controller and auditor general, HC 297, Session 2009-2010*.

National Institute for Health and Clinical Excellence (NICE) (2010). *Pregnancy and complex social factors: A model for service provision for pregnant women with complex social factors* . National Collaborating Centre for Women's and Children's Health. Royal College of Obstetricians and Gynaecologists.

National Institute for Health and Clinical Excellence (NICE) (2007). *Methadone and buprenorphine for the management of opioid dependence.* (Rep. No. Technology appraisal guidance 114).

New South Wales Department of Health (2006). *National clinical guidelines for the management of drug use during pregnancy, birth and the early development years of the newborn*. North Sydney, Australia: Ministerial Council on Drug Strategy.

Nunn, A., Zaller, N., Dickman, S., Trimbur, C., Nijhawan, A., & Rich, J. D. (2009). Methadone and buprenorphine prescribing and referral practices in US prison systems: results from a nationwide survey. *Drug and Alcohol Dependence, 105,* 83-88.

Rementeria, J. L. & Nunag, N. N. (1973). Narcotic withdrawal in pregnancy: stillbirth incidence with a case report. *Am.J Obstet.Gynecol., 116,* 1152-1156.

Siegel, S. & Castellan, N. J. (1988). Nonparametric Statistics for the Behavioral Sciences. In (2nd ed., pp. 123). New York: McGraw-Hill.

Sitzia, J. & Wood, N. (1998). Response rate in patient satisfaction research: an analysis of 210 published studies. *Int.J Qual.Health Care, 10,* 311-317.

Unger, A., Jagsch, R., Jones, H., Arria, A., Leitich, H., Rohrmeister, K. et al. (2011). Randomized controlled trials in pregnancy: scientific and ethical aspects. Exposure to different opioid medications during pregnancy in an intra-individual comparison. *Addiction, 106,* 1355-1362.

Winklbaur, B., Kopf, N., Ebner, N., Jung, E., Thau, K., & Fischer, G. (2008). Treating pregnant women dependent on opioids is not the same as treating pregnancy and opioid dependence: a knowledge synthesis for better treatment for women and neonates. *Addiction, 103,* 1429-1440.

Wittmann, B. K. & Segal, S. (1991). A comparison of the effects of single- and split-dose methadone administration on the fetus: ultrasound evaluation. *International Journal of the Addictions, 26,* 213-218.

Wolff, K., Boys, A., Rostami-Hodjegan, A., Hay, A., & Raistrick, D. (2005). Changes to methadone clearance during pregnancy. *Eur.J.Clin.Pharmacol., 61,* 763-768.

Young, D. M. (2007). Management of Opioid Dependence in Pregnancy: A Review of the Evidence. *International Journal of Mental Health and Addiction, 5,* 187-194.

Zuspan, F. P., Gumpel, J. A., Mejia-Zelaya, A., Madden, J., & Davis, R. (1975). Fetal stress from methadone withdrawal. *Am.J Obstet.Gynecol., 122,* 43-46.

Table 1

Response rates from community drug treatment services (CDTS) by regions in England & Wales

London	65.6% (21/38)	East Midlands	58.3% (7/12)
South West	81.8% (9/11)	Yorkshire & Humber	77.0% (20/26)
South East	65.6% (21/32)	North East	94.7% (18/19)
East Anglia	65.0% (13/20)	North West	52.3% (22/42)
West Midlands	66.7% (14/21)	Wales	75.0% (9/12)
England & Wales 66.1% (154/233)			

Note: The response rates represent the proportion of respondents from the total of community drug treatment services (CDTS) identified in each region.

Figure 1

Treatment options offered to pregnant opioid dependent users by community drug treatment services (CDTS) in England and Wales

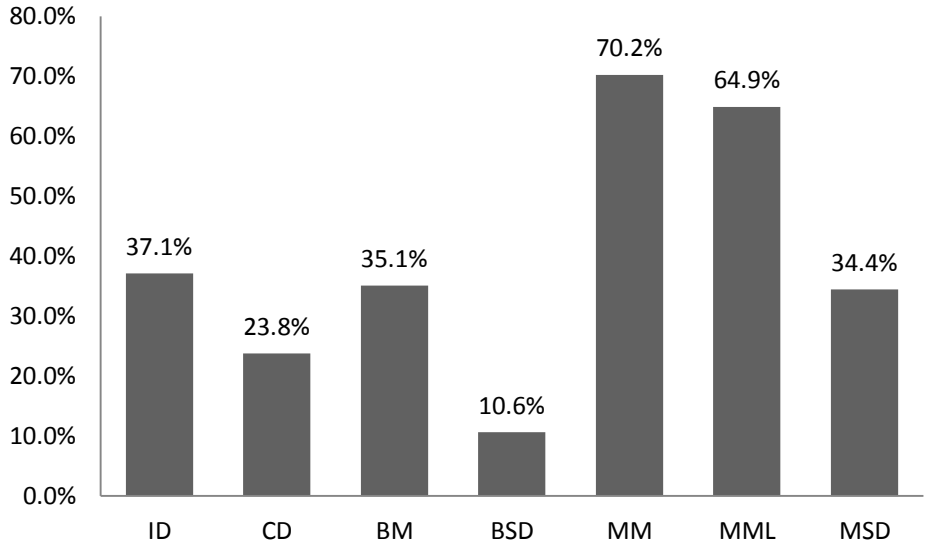

Figure 1. Percentage of community drug treatment services (CDTS, N=154) offering different treatment options to pregnant opioid users. ID= Inpatient Detoxification; CD= Community Detoxification; BM= Buprenorphine Maintenance; BSD= Buprenorphine Stabilisation following by Detoxification; MM= Methadone Maintenance; MML=Methadone Maintenance Low dose; MSD= Methadone Stabilisation followed by Detoxification.

*Title Page

A national survey investigating methadone treatment for pregnant opioid dependent women

Raul Perez-Montejano, Emily Finch and Kim Wolff

King's College, London

Author Note

Raul Perez-Montejano, Department of Mental Health, Tees Esk and Wear Valleys NHS Foundation Trust, Northallerton, United Kingdom

Emily Finch, South London and Maudsley NHS Foundation Trust, London, United Kingdom

Kim Wolff, King's College London, Institute of Pharmaceutical Sciences, London, United Kingdom

Conflict of interest: Authors have not received any funding support from any company or organisation for the submitted manuscript.

Data Analysis: Authors have full access to the data and jointly take responsibilities for the integrity of the data analysis which was submitted in completion of a PhD thesis. Authors agree to allow the data to be reviewed if requested.

Correspondence concerning this article should be addressed to Dr Raul Perez-Montejano, Department of Mental Health, Friarage Hospital, Tees Esk and Wear Valleys NHS Foundation Trust, Northallerton, United Kingdom. Email: r.perez@nhs.net Tel: 00 44[0] 1609 763267 Fax: 00 44[0] 1609 7